REMARKS

I. Disposition of the Claims

Claims 26, 29-35, and 40-42 are all the claims pending in the application. Claims 26 and 29 are currently amended. Claims 41 and 42 are newly submitted.

Claim 26 has been amended, in part, to clarify that the previously recited steps of the sequencing of a portion of the target nucleic acid molecule and the determination of the position of said portion within the target molecule can be carried out in any order. Support for the amended claim can be found throughout the specification, for example, in the original claims. Claim **26** has also been amended to recite that the label is "associated with said portion of the target nucleic acid molecule", which is supported in Example 21 (page 95, lines **28-00**). For clarity, claim **26** has been amended to recite that the label which indicates the position of said portion within the target nucleic acid molecule is not used to determine the sequence of said portion, (see Example 21, page 95, lines **28-00**). Finally, new claim **26** has also been amended to recite that the portion which is sequenced has 2 or more bases, which is supported on page 7, lines 11-14.

Claim 29 has been amended for clarity. Support for the amended claim can be found throughout the specification, for example, in the original claims.

New claims 41 and 42 have been submitted. Support for the new claims can be found, for example, in original claim 26, Example 21 on page 95, and in Figure 20.

No new matter has been added.

II. Novelty

The Examiner has rejected claims 26, 39-35 and 40 under 35 USC 102(b) as being anticipated by Brenner et al. (US 5,552,278), with particular reference to the disclosure in Example 1.

Example 1 of Brenner discloses a method of sequencing an amplified target polynucleotide comprising digesting the target polynucleotide with a restriction enzyme to create a 5' overhang and then incubating the target polynucleotide with four separate fluorescent probes, each of which produces a characteristic fluorescence when ligated to one of the four nucleotide bases. Each probe comprises a 3' overhang —XNNN, wherein X is the nucleotide that is specific for the particular probe (either A, T, G or C), and N is any one of the four nucleotides. Therefore, following incubation, the 3' overhang of the fluorescent probe will hybridize to the 5' overhang of the target, if the bases within the two overhangs are complementary, resulting in the probe emitting its characteristic fluorescence. Since the identity of nucleotide X is known, the identity of the base on the target to which it hybridizes (the 5'-terminal nucleotide) can be determined by observing which of the four probes fluoresces following incubation with the target. The litigation complex formed between the target and the probe is then incubated with an endonuclease and the sequenced nucleotide is cleaved, exposing a new 5'-terminal base (the base at position two in the original target polynucleotide), which can be identified by repeating the cycle of probe litigation and cleavage.

This method differs from the method of the claimed invention in a number of ways. Firstly, the "portion" of the target that is sequenced according to the Brenner method is only a single nucleotide per sequencing cycle, since each round of sequencing identifies only the 5'-terminal base. In contrast, claims 26 and 42 state that the portion which is sequenced has 2 or more bases, and, as noted in the specification (page 7, line 14) can comprise up to 20 bases.

Furthermore, the Brenner method does not utilize a label which is associated with the portion of the nucleic acid molecule to be sequenced in order to identify the position of this portion within the target molecule. At best, minimal positional information is derivable from the Brenner method, since the base that is sequenced always corresponds to the nucleotide at the 5'-end. The method is restricted to determining the identity of the nucleotide at this position only. Unlike the method of the present invention, the Brenner method can not be used to identify the sequence or position of a portion located within the target sequence. Furthermore, the fluorescent label which is used in the Brenner method does not equate to the positional label of the claimed invention. In the Brenner method, a single probe is utilized to both sequence the portion and determine its location within the target. This differs from the method of the present claims, wherein the label which indicates the position of the portion within the target molecule is not used to determine the sequence of said portion. Consequently, Brenner cannot be said to anticipate the claims of the present invention, which should be recognized as being novel.

The claimed method is technically advantageous over the method disclosed by Brenner as it is enables faster sequencing of all or part of the target molecule by identifying the sequence and position of larger portions (of up to 20 bases) in each cycle of analysis. Referring to the

specific example provided in the Brenner publication, four rounds of sequencing/cleavage would be required in order to sequence the 4 base overhang of SEQ ID No. 3. In contrast, these 4-bases portions could be sequenced, and the position of the 4-base portion within the target molecule identified, in a single analytical cycle using the method of the invention. Using the Brenner method, it is not possible to achieve this because of the number of unique fluorescent signals required. As detailed in Example 1, four colored probes are needed to accurately identify a single base pair, and the number of probes requires increases exponentially as the number of base pairs to be sequenced increases.

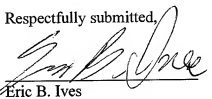
Furthermore, the claimed method is also more flexible than the Brenner method, as it is not limited to determining the sequence from the end of the target molecule; it can be used to analyze the sequence of portions located within a target sequence. Therefore, the skilled reader of the Brenner publication would not be able to arrive at the claimed invention without making substantial changes to the method, requiring significant inventive activity.

III Conclusion

In view of the above, reconsideration and allowance of this application are now believed to be in order, and such actions are hereby solicited. If any points remain in issue which the Examiner feels may be best resolved through a personal or telephone interview, the Examiner is kindly requested to contact the undersigned at the telephone number listed below.

The USPTO is directed and authorized to charge all required fees, except for the Issue Fee and the Publication Fee, to Deposit Account No. 19-4880. Please also credit any overpayments to said Deposit Account.

Respectfully submitted,



Eric B. Ives
Registration No. 50,928

SUGHRUE MION, PLLC
Telephone: (202) 293-7060
Facsimile: (202) 293-7860
WASHINGTON OFFICE
23373
CUSTOMER NUMBER

Date: 7-1-2010